UNITED STATES DEPARTMENT OF COMMERCE
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KM

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/151,612	09/11/98	KOHN	L 5616/3

HM12/0119

ROGERS & WELLS
200 PARK AVENUE
NEW YORK NY 10166-0153

EXAMINER	
NGUYEN, D	
ART UNIT	**PAPER NUMBER**
1632	12

DATE MAILED: 01/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/151,612	KOHN ET AL.	
	Examiner	Art Unit	
	Quang Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-18,21-26,29-35,42-46,60,62 and 74-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-18,21-26,29-35,42-46,62,74-76 and 78-80* is/are rejected.

7)☒ Claim(s) *77* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

Applicant's amendment filed on 01 November 2000 in Paper No. 11 has been entered. Originally filed and amended claims 1-2, 4-18, 21-26, 29-35, 42-46, 60, 62 and 74-80 are pending in the present application.

References cited in the IDS have not been considered because they were unavailable at the time of examination.

The present application has been transferred to a new examiner, and upon reviewing the instant application the following is a new ground of rejection for the originally filed, amended and newly added pending claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 4, 6, 7, 9-13, 15, 17, 18, 23-26, 42, 43 and 44 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a method of increasing immune recognition of a mammalian cell by introducing a sequence non-specific double-stranded polynucleotide greater than 25 nucleotides in length into the cell and thereby activating expression of a gene or gene product that increases immune recognition gene or gene product, peptide processing genes or gene products, Class II regulatory genes and gene products, co-stimulatory molecule gene or gene products, wherein such activation is involved in

antigen presentation, growth and function of the cell and which increases the ability of a cell to present antigen to an immune cell. The claimed method is indistinguishable from naturally occurring viral or bacterial infection processes and a naturally occurring injury process causing the leakage of self DNA fragments into the cell cytoplasm.

Claim Objections

Claim 77 is objected to because of the following informalities: the phrase "with the an effective amount" is not proper. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-18, 21-26, 29-35, 42-46, 74 and 75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *in vitro* method of increasing immune recognition of a mammalian cell by introducing a sequence non-specific double stranded polynucleotide greater than 25 nucleotides in length into the cell and thereby activating expression of MHC class I and class II genes or gene products, peptide processing genes or gene products consisting of TAP-1, TAP-2 and a proteosome subunit, Class II regulatory genes or gene products consisting of HLA-DM and invariant chain, co-stimulatory molecule genes or gene products consisting of B7 so-stimulatory molecule, PKR, IFN-beta, MAP kinase, NF-κB and JAK,

or a STATs activation involved in antigen presentation, growth and function of the cell and increases the ability of a cell to present antigen to an immune cell; and a method for inducing an autoimmune disease mimicking the human Graves' disease in a mouse, said method comprises introducing a sequence non-specific double stranded polynucleotide greater than 25 nucleotides in length into a syngeneic murine cell *in vitro*, and introducing said murine cell into the host mouse, does not reasonably provide enablement for other embodiments in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

Claims 1, 2, 4-18, 21-26 and 42-45 are directed to a method of increasing immune recognition of a mammalian cell by introducing a sequence non-specific double stranded polynucleotide greater than 25 nucleotides in length into the cell and thereby activating expression of a gene or gene product that increases immune recognition.

Claims 74, 75, 29-35 and 46 are drawn to a method for increasing presentation of antigen by a cell comprising: (a) introducing a sequence non-specific double-stranded polynucleotide greater than 25 nucleotides in length into the mammalian cell

ex vivo, which causes the cell to have an increased ability to present antigen and measuring an increase in expression of MHC molecules or co-stimulatory molecules, or MHC molecules and co-stimulatory molecules involved in antigen presentation selected from the group consisting of TAP-1, TAP-2, a proteosome subunit, HLA-DM, invariant chain, CIITA, RFX5, B7 co-stimulatory molecule, PKR, IFN-beta, MAP kinase, NF-κB, JAK and a STAT.

The specification teaches that any double stranded (ds) nucleic acid fragment introduced *in vitro* into the cytoplasm of non-immune cells or leakage of self DNA caused by environmentally induced damage can induce MHC gene expression directly and the expression of other essential genes and gene products important for antigen processing and antigen presentation. The effect is sequence-independent, is not duplicated by single stranded nucleic acids, and it is different and additive to that of γIFN. The specification further discloses that ds-polynucleotides can induce the expression of the 90K tumor-associated immunostimulator implicated in host mechanisms to defend against tumors and AIDS, and that ds-polynucleotides regulate cell cycle progression and growth, and their regulation mechanism is different from that of γIFN. Additionally, the specification teaches that mice immunizing with syngeneic fibroblasts transfected *in vitro* with ds-polynucleotides and a functional thyrotropin receptor (TSHR), were induced to develop an autoimmune disease with features mimicking the human Grave's disease.

The above evidence is noted and considered. However, the evidence can not be extrapolated to the instant broadly claimed invention which when read in light of the

specification encompass an *in vivo* method of increasing immune recognition of a mammalian cell by introducing a sequence non-specific double stranded polynucleotide greater than 25 nucleotides in length into a cell and an *ex vivo* method of increasing presentation of antigen by a cell for immunization purpose to treat various autoimmune conditions or diseases, among which is cancer (See specification, page bottom paragraph of page 44 to the top paragraph of page 45, and claims 26, 45, 75 and 29-35).

The specification is not enabled for the broadly claimed invention because the specification fails to provide guidance or direction for a skilled artisan to deliver *in vivo* a sequence non-specific double stranded polynucleotide greater than 25 nucleotides in length into a cell in a host to induce an effective immune response for immunization purposes or for producing any and all autoimmune reactions. Nor does the specification provide sufficient guidance for an *ex vivo* method to induce an effective immune response in a host for recognizing and killing tumor cells. The specification does not teach the dosage amounts, frequency, or routes of administering ds-polynucleotides or cells transfected with ds-polynucleotides into a host to generate desired therapeutic results for any specific autoimmune conditions or diseases. The mere upregulation of MHC, genes and gene products involved in antigen processing and antigen presentation, and 90K tumor-associated immunostimulator by ds-polynucleotides in cells *in vitro* and the generation of mice having an autoimmune disease with features mimicking the human Grave's disease are not deemed to correlate with any protective or therapeutic immune responses. Since the prior art does not teach such a correlation,

it is incumbent upon the instant application to do so. In the absence of such a guidance, it would have required undue experimentation without an expectation of success for one skilled in the art to make and use the claimed invention.

With respect to claims encompassing an *in vivo* method, the nature of the claims falls within the realm of genetic immunization which at the effective filing date of the present application was still immature and highly unpredictable. Regarding to the state of the art of genetic vaccines, Chattergoon et al. (FASEB J. 11:753-763, 1997) noted that although DNA vaccines have shown promises in animal models and have raised hopes, the technology is still considered to be an "emerging" technology (column 1, paragraphs 2 & 3, page 762). In addition, Chattergoon et al. stated that "there is little evidence that the immune response induced by these vaccines will be completely protective against any human pathogen (page 762, paragraph bridging columns 1-2). More recently, Leitner et al. (Vaccine 18:765-777, 2000) stated that "Although genetic vaccines have been significantly improved, they may not be sufficiently immunogenic for therapeutic vaccination of patients with infectious disease or cancer in clinical trials" (Abstract, page 765). It is well recognized that the animal model should correlate to the disease condition studied, and the route of administration as being a critical parameter determining whether protective immunity is elicited. One of skilled in the art would have also have recognized that results observed in animal model systems are not predictive of outcome or efficacy in applications in other species of animal or in humans, due to differences in anatomy, cell biology, genetics and immunology between different types of animals, and between the animal models and humans (See page 79 in Ledley F.D.,

Hum. Gen. Ther. 2:77-83, 1991). This is further supported by the teachings of McCluskie et al. (Mol. Med. 5:287-300, 1999) who stated that "it is probably safe to say that any vaccine that works in a human will work in a mouse, but not necessarily vice versa. Therefore, it is difficult to predict from mouse studies the potential of a new vaccine for humans. In fact, in those human trials that have carried out, none of the DNA vaccines induced the strong immune responses that had been seen in mice with the same vectors." (column 2, last paragraph, page 296). The sequence non-specific double-stranded polynucleotides recited in the instant claims would encompass any and all vectors used in the cited arts. As noted previously, the disclosures of the instant specification are not correlated to the effective protective immune responses to be induced or the desired therapeutic results hoped to be achieved by the claimed method. Nor does the specification provide any guidance demonstrating that the claimed method would be effective in any and all subjects. In the absence of such teachings provided by the instant specification, it would have required undue experimentation without a predictable expectation of success for one skilled in the art to make and use the claimed invention.

An embodiment of the claims encompassing an *in vivo* method requires the introduction of a ds-polynucleotide into a particular cell (cell expressing an autoantigen, see claim 12) or specific cell types (non-immune cell, immune cell, antigen presenting cell, thyroid cell or tumor cell, see claims 13 and 75). However, the specification fails to provide any guidance regarding to the delivery of a sequence non-specific ds-polynucleotide to a specific target cell or a specific cell population. Vector targeting *in*

vivo to desired cells or organs continues to be unpredictable and inefficient. This is supported by numerous teachings in the art. Deonarain (Exp. Opin. Ther. Patents 8:53-69, 1998) indicated that one of the main obstacles hampering a successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time." (page 53, first paragraph). Deonarain also reviewed new techniques under experimentation in the art which show promises. One of which is the ligand-targeted receptor-mediated vector approach with a relatively higher level of tissue specificity than viruses can offer. However, this approach to gene therapy is much less efficient than viral gene delivery (column 1, last paragraph, page 65). Verma & Somia (Nature 389:239-242,1997) reviewed various vectors known in the art for use in gene therapy, and the problems which are associated with each. They also indicated clearly that resolution to vector targeting had not been achieved in the art (see the entire article). Verma & Somia also discussed the role of the immune system in inhibiting the efficient targeting of viral vectors such that an efficient delivery of a transgene, for this instance a ds-polynucleotide, is not achieved (see page 239, and second and third columns of page 242). The instant specification fails to teach one of skill in the art how to overcome the unpredictability for vector targeting or more specifically the delivery of a non-sequence specific ds-polynucleotide to targeted cells can be achieved by any mode of delivery to yield desired induced immune responses. Since the prior art does not provide such guidance nor the instant specification supply such teaching, it would therefore have required undue

experimentation without a predictable expectation of success for one skilled in the art to make and use the claimed invention.

With regard to claims drawn to an *ex vivo* method, there are several questions that need to be addressed, such as, "What is the minimum proportion of cells or tumor cells transfected with a sequence non-specific ds-polynucleotide required to induce an effective protective or therapeutic immune response, or a desired autoimmune response in a host to generate various models for specific autoimmune conditions or diseases?", "To which host tissues do transfected cells home in and how long do they need to stay in the system of the host to induce desired immune responses?", "Which route of delivery of these transfected cells is effective to obtain the desired immune responses?", "How stable is the state of activated antigen presenting for cells transfected with a nonsequence specific ds-polynucleotide?" . The specification fails to provide teachings regarding to the issues raised above and it does not supply any guidance demonstrating that any therapeutic or protective immune response has been actually achieved by the claimed method. Given the lack of guidance and direction provided by the instant specification, it would therefore require undue experimentation without a predictable expectation of success for a skilled artisan to make and use the broadly claimed invention.

Lastly, apart from the teachings provided by the instant specification regarding to the generation of a mouse model having features mimicking the human autoimmune Graves' disease, the specification fails to provide sufficient guidance or direction for the generation of any and all other autoimmune disease models. Relevant information such

as the specific co-transfected gene encoding for an antigen (thyrotropin receptor for the disclosed mouse model), the promoter, the vector construct used to express said antigen, the cell dosage used, the frequency and route of administering utilized to generate other specific autoimmune disease models are absent. It should be noted that guidance for overcoming known differences in anatomy, cell biology, genetics and immunology between different types of animals has not been provided by the instant specification for making any and all animal models with desired autoimmune diseases. Moreover, The CAFC has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The Appeal court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genetech, Inc. v. Novo Nordisk A/S*, 42 USPQ 2d 1001, at 1005).

Accordingly, due to the lack of direction and guidance provided by the specification, the unpredictability of the genetic immunization art, and the breadth of the claims, it would have required undue experimentation without a predictable degree of success for one skilled in the art to make and use the instant broadly claimed invention.

Claims 60, 62 and 76-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 60 and 62 are drawn to a method for treating cancer or an infectious disease caused by a virus, bacteria, yeast, protozoa, a disease caused by environmental injury or an autoimmune disease sensitive to immunotherapy which comprises: (a) removing diseased cells from a mammal; (b) introducing a sequence non-specific double stranded polynucleotide greater than 25 nucleotides in length into the cells; (c) treating the cells to prevent division but permits other metabolic activity; and (d) immunizing the mammal with an effective amount of the cells to prevent or alleviate the symptoms of the disease; the same method used in conjunction with other treatment methods to enhance therapeutic results.

Claim 76 is directed to a vaccine for treating cancer, artherosclerosis, an autoimmune disease, or an infectious disease caused by a virus, bacteria, yeast, protozoa, comprising a somatic mammalian cell with the enhanced ability to present antigen to the immune system comprising: (a) introducing a sequence non-specific double stranded polynucleotide greater than 25 nucleotides in length into the somatic mammalian cell *ex vivo*, which causes the cell to have an increased ability to present antigen; (b) measuring an increase in expression of MHC molecules or co-stimulatory molecules involved in antigen presentation selected from the group consisting of TAP-1, TAP-2, a proteosome subunit, HLA-DM, invariant chain, CIITA, RFX5, B7 co-stimulatory molecule, PKR, IFN-beta, MAP kinase, NFκB, JAK and a STAT; and (c) preparing the mammalian cell for immunization.

Claims 77-80 are directed to a method for treating cancer, artherosclerosis, an infectious disease caused by a virus, bacteria, yeast, protozoa, a disease caused by environmental injury or an autoimmune disease sensitive to immunotherapy which comprises: (a) removing diseased cells from a mammal; (b) increasing or decreasing the expression of antigen by the cell; and (c) immunizing the mammal with an effective amount of the cell to prevent or alleviate the symptoms of the disease.

The specification is not enabled for the claimed invention for the same reasons already set forth in the rejection of claims 1, 2, 4-18, 21-26, 29-35, 42-46, 74 and 75 above. Basically, the specification fails to provide guidance and direction for a skilled artisan to obtain any therapeutic effects for any specific diseases using the method or using the vaccine of the present invention as claimed. Relevant issues regarding to the claimed method have not been adequately addressed by the instant specification as outlined previously. As another example, with regard to claim 77, the specification fails to teach specifically the parameters involved in the increasing or decreasing expression of an antigen in a cell, a particular antigen for a specific disease to be treated in the claimed method. In addition, the complex nature of the cytokine network and its interaction between various immune cells which play an integral part of augmenting the effector function to yield therapeutic effects in an immunotherapy are not readily predictable. The physiological art has been recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad

> enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictablity of factors involved.

Accordingly, given the failure of the instant specification to provide the specifics for carrying out the claimed method and use of the claimed vaccine for any of the numerous claimed diseases, it would have required undue experimentation without a predictable expectation of success for a skilled artisan to make and use the claimed invention.

In response to the previous Office Action mailed on 04/26/00, Applicant mainly argued that since the instant invention does not describe or claim methods for gene therapy in humans or otherwise, and therefore the rejection for the lack of enablement based on a failure to enable a gene therapy is not appropriate. The examiner respectfully finds Applicant's argument to be unpersuasive for the following reasons. Although, the instant claimed invention does not require the expression of a transgene as rightfully pointed out by the Applicant, however, the scope of the pending claims encompasses certain aspects of a gene therapy, such as the requirement for an efficient *in vivo* delivery of a ds-polynucleotide to certain target cells to induce desired therapeutic immune responses, and the need for an effective route of administration and effective dosages of ds-polynucleotides or cells transfected with ds-polynucleotides into a host to achieve desired therapeutic results as discussed above. Therefore, the claimed invention is also subjected to the unpredictability of the gene therapy art, and there is a need for sufficient guidance or direction provided by the specification for a

skilled artisan to make and use the instant claimed invention. Additionally, the response is not adequate in light of a new ground of rejection set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-18, 21-26, 29-35, 42-46, 62, 74-76 and 78-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the phrase "expression of a gene, or gene and gene product, or gene product" is unclear and it seems to be redundant. The expression of a gene results in a gene product. Clarification is needed. Also in claim 1, there is an improper Markush language recited as "peptide processing genes or gene products consisting of TAP-1, TAP-2, a proteosome subunit, Class II regulatory genes and gene products". Do Class II regulatory genes or gene products include in the group of peptide processing genes or gene products? The term "a STATs activation" is unclear, it does not represent a gene or a gene product in the recited group of the co-stimulatory gene or gene products. Clarification is needed. Moreover, the term "such activation" on the next to last line of the claim is unclear. Which activation? Is it a STATs activation or the activation of the expression of a gene and gene product that increases immune recognition gene?

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since

the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "gene or gene product that increases immune recognition gene" and the claim also recites "MHC class I and class II genes", "peptide processing genes or gene products", "Class II regulatory genes or gene products", "co-stimulatory gene or gene products", which are the narrower statement of the range/limitation.

Claim 2 and its dependent claims 15-18 and 24 recite the limitation "the molecule" in line 1 of the claim. There is insufficient antecedent basis for this limitation in the claim. Which molecule? The molecule is not recited in claim 1 on which claim 2 is dependent upon. Clarification is needed.

In claim 7, the phrase "an exogenous or environmental stimulus" is unclear and since the specification does not define the recited exogenous or environmental stimulus, the metes and bounds of the claim can not be determined exactly.

Claims 32 and 34 recite the limitation "activated APC" in line 2 of the claims. There is insufficient antecedent basis for this limitation in the claim. There is no recitation of activated APC in claims 75 and 74 from which claims 32 and 34 are dependent upon, respectively.

In claim 46, it is confusing and unclear whether the claim is directed to a composition or to a method because method steps are recited in the claim. For the purpose of a compact prosecution, it is interpreted as a method claim.

Similarly, it is unclear whether claim 76 is drawn to a vaccine or a method of vaccination because the claim recites method steps. For the purpose of a compact prosecution, it is interpreted as a method claim. As such, claim 76 is incomplete because it lacks a step or steps connecting the recited steps (a) to (c) to treating cancer, artherosclerosis, an autoimmune disease, or an infectious disease caused by a virus, bacteria, yeast, protozoa recited in the preamble of the claim.

Claim 74 is incomplete because it lacks a step or steps connecting the recited step to increasing presentation of antigen recited in the preamble of the claim. Additionally, claim 74 recites the broad recitation "MHC molecules or co-stimulatory molecules", and the claim also recites "TAP-1, TAP-2, a proteosome subunit, ...", which is the narrower statement of the range/limitation.

In claims 62 and 78, the phrase "enhance other treatment methods" is unclear and therefore it renders the claim indefinite. Which other treatment methods? Moreover, what does enhancing other treatment methods mean? Do Applicant mean to obtain additional or synergistic therapeutic effects regarding to the preventing and

alleviation of the symptoms of the disease? The metes and bounds of the claims can not be determined exactly if the claim language is not clear.

Claims 79 recites the limitation "activation or maturation of dendritic cells or peripheral blood macrophages" in lines 1 and 2 of the claim. There is insufficient antecedent basis for this limitation in the claim. In claims 77 and 78 from which claim 79 is dependent on, there is no recitation of dendritic cells or peripheral blood macrophages, but only of diseased cells removed from a mammal.

Claim 80 recites the limitation "somatic cells" and "CpG residues" in lines 1 and 2 of the claim. There is insufficient antecedent basis for this limitation in the claim. In claims 77 and 78 from which claim 80 is dependent on, there is no recitation of somatic cells or CpG residues, but only of diseased cells removed from a mammal.

Conclusions

Claims 1-2, 4-18, 21-26, 29-35, 42-46, 60, 62 and 74-80 are free of prior art. At the time of the instant invention, the prior art did not teach or fairly suggest the claimed invention of the present application.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Deborah Crouch, Ph.D., may be reached at (703) 308-1126, or SPE, Karen Hauda, at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Patsy Zimmerman, whose telephone number is (703) 305-2758.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1632.

Papers related to this application may be submitted to Group 160 by facsimile transmission. Papers should be faxed to Group 160 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The CM1 Fax Center number is or (703) 305-3014 or (703) 308-4242.

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800 1630

Quang Nguyen, Ph.D.
Examiner, AU 1632